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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/825,867

04/16/2004

Jason W. Chin

54A-000240US

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22798

7590

08/29/2008

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EXAMINER

GEBREYESUS, KAGNEW H

ART UNIT

PAPER NUMBER

1656

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/825,867	<b>Applicant(s)</b> CHIN ET AL.	
	<b>Examiner</b> KAGNEW H. GEBREYESUS	<b>Art Unit</b> 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 6/23/08.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 38,39,41,42,47,50-57,131-133,144-147 and 149-151 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 38,39,41,42,47,50-57,131-133,144-147 and 149-151 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 23, 2008 has been entered. Claims 38-42, 47, 50-57, 131-133, 144-147, and 149-151 are pending with this amendment. Claims 38, 39, 42 and 131-133 are amended.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38, 39, 41, 42, 47, 50-57, 131-133, 144-147 and 149-151 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 39, 41, 42, 47, 50-57, 131-133 and 149-151 are rejected for the recitation "analogue thereof" because it is not clear if these unnatural amino acids are structural and/or functional analogues or what function these analogues have. The metes and bounds of this term are not clear. For examination purposes, this recitation encompasses any unnatural amino acid.

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Furthermore claims 38, 144-147 are rejected because of the recitation “at least 90% identical to a Gal4 from *Saccharomyces cerevisiae*”. The recitation of at least 90% to identical” is relative to any Gal4 from the genus of Gal4 comprised in the recitation “a Gal4 from *Saccharomyces cerevisiae* which is understood as having a wild type DNA binding domain and wild type DNA activation domain while the rest of the protein structure is not necessarily wild type. Applicants are advised to identify the sequence with a SEQ ID NO for clarity.

***Withdrawn - Claim Rejections - 35 USC § 112***

Claim 148 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is withdrawn following the cancellation of the claim.

***Maintained - Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39, 41, 42, 47, 50-57, 131-133 and 149-151 are rejected under 35 U.S.C. 112, first paragraph. The specification is not enabled for any recombinant protein comprising any number of unnatural amino acids or keto amino acids that are further modified post translationally.

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The response argues:

“The rejection acknowledges that claim 38 is enabled for adding or substituting unnatural amino acids, but alleges that the claims were overbroad for including too many possible variants. In a sincere effort at advancing prosecution, Applicants have amended claim 38 to recite that the protein is at least 90% identical to the wild-type GAL 4. The claim also includes the limitations that the protein include a full-length wild-type N-terminal DNA binding domain and a full-length wild-type C-terminal activation domain. The claim further includes the limitation that the recombinant mutant GAL4 protein is capable of activating a GAL4 responsive gene”.

Applicant's argument has been carefully considered but found persuasive. The scope of enablement rejection with respect to Claims 38, 146, and 147 is withdrawn.

The claims encompass any recombinant protein comprising any number of p-acety-L-phenylalanine, p-amino-L-phenylalanine, p-azido-L-phenylalanine or any analogue thereof (this term is indefinite therefore any unnatural amino acid. see rejection under 35 U.S.C. 112, second paragraph for lack of clarity below). However the specification does not teach how to make and use the invention commensurate in scope with the claims because the specification does not teach how to produce a protein comprising any number of p-acety-L-phenylalanine, p-amino-L-phenylalanine, p-azido-L-phenylalanine or any analogue thereof and/or perform a posttranslational modification on all possible unnatural amino acid analogues.

Furthermore claims 42, 47, 50-57, 131-133, 151 encompass any protein or a protein derived from a naturally occurring EPO, IFN-beta, Factor VII or any antibody (151) comprising any number of p-acety-L-phenylalanine, p-amino-L-phenylalanine, p-azido-L-

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phenylalanine or any analogue thereof (therefore type of unnatural amino acid) that are further modified by various types of post-translational modifications. However, the specification does not teach how to make and use the invention commensurate in scope with these claims because the specification does not teach which unnatural amino acids when incorporated can further be modified by phosphorylation, lipid- modification, palmitoylation, palmitate addition and a glycolipid-linkage modification.

The specification does not provide guidance for the scope of the term "an analogue" and one of skill would not know how to make a protein comprising said "analogue" or the specific ORS/OtRNA required to incorporate said analogue into a protein and further modify it post-translationally.

Claims 139-143:

The rejection of these claims is withdrawn following cancellation of the claims.

***Claim Rejections - 35 USC § 103***

Claims 39, 41-42, 47, 50-57, 131-133 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al (US 20050186657 A1 now US 7,129,333 B2). Schultz et al teach compositions comprising a protein (glycoprotein) wherein at least one unnatural amino acid such as para-acetyl-L-phenylalanine (a keto-amino acid) is incorporated into said protein and which is further modified with saccharide moieties. Schultz et al teach that in order for a eukaryotic system to be used, the vectors optionally comprise generic expression cassettes containing at least one independent terminator sequence,

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sequences permitting replication of the cassette in eukaryotes, or prokaryotes, or both (e.g., shuttle vectors) and selection markers for both prokaryotic and eukaryotic systems. Claims 39, 41-42, 131-133 are obvious over Schultz et al because they teach glycoprotein mimetics produced by incorporating a p-acetyl-phenylalanine that is further post-translationally modified with saccharide moieties.

Furthermore in paragraph [0083] Schultz et al teach that the composition includes at least one protein with at least one, e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, or at least ten or more unnatural amino acids, e.g., an unnatural amino acid comprising a moiety where a saccharide moiety can be attached, or an unnatural amino acid that includes a saccharide moiety, and/or which include another unnatural amino acid. The unnatural amino acids can be the same or different, (limitations in claims 50-53).

In paragraph [0081] Schultz et al teach that the composition optionally includes, e.g., at least 10 micrograms, at least 50 micrograms, at least 75 micrograms, at least 100 micrograms, at least 200 micrograms, at least 250 micrograms, at least 500 micrograms, at least 1 milligram, at least 10 milligrams or more of the glycoprotein, or an amount that can be achieved with in vivo protein production methods, were said protein is found in, e.g., a cell lysate, a buffer, a pharmaceutical buffer, or other liquid suspensions (limitations in claims 54-56). Furthermore [0288] of Schultz et al teaches that a polyhistidine tag is attached to facilitate the purification of the protein (myoglobin) comprising the unnatural amino acid (limitation in claim 57).

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Schultz et al do not specifically teach a specific protein composition comprising the at least one unnatural amino acid with posttranslational modification AND where the protein additionally comprises an oligosaccharide covalently coupled to an asparagine, threonine or serine residue of the protein. However it would have been obvious for a person of ordinary skill in the art to further modify the protein in view of designing desired glycosylated proteins as these post-translational modifications affect a wide range of protein functions from folding and secretion to biomolecular recognition and serum half life. ([0280]).

Furthermore claims 42, and dependent claims thereof recite a composition comprising a protein wherein the modification is selected from the group consisting of: phosphorylation, lipid-modification, palmitoylation, palmitate addition and a glycolipid-linkage modification or where residues Asn, Thr or Ser are further modified. However, it would have been obvious for a person of ordinary skill in the art to produce any naturally occurring eukaryotic protein comprising the above naturally occurring modifications in a purified form as suggested by Schultz et al in paragraph [0280] under example 4.

One of skill in the art would have a reasonable expectation of success because post-translational modifications are normal physiological processes in eukaryotic cells.

**Conclusion:** No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone



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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kagnew H Gebreyesus PhD/  
Examiner, Art Unit 1656

/Kathleen Kerr Bragdon/  
Supervisory Patent Examiner, Art Unit 1656